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10/815,652	04/02/2004	Tadashi Hayashi	00862.018048.	8200
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EXAMINER				
BOWERS, NATHAN ANDREW				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary**Application No.**

10/815,652

Applicant(s)

HAYASHI, TADASHI

Examiner

NATHAN A. BOWERS

Art Unit

1797

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 7, 9, 11 and 13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 7, 9, 11 and 13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SI-08)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date _____

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1) Claims 1, 9, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gruber (US 20030119177) in view of Griner (US 5266272) and either Huang (US 20040146849) or Xu (US 7470533).

With respect to claims 1 and 13, Gruber discloses a target object modification apparatus and method that includes the use of an aligner device for producing an optical trap capable of manipulating the posture of a supplied target modification minute object within a reaction chamber. This is disclosed in paragraphs [0015]-[0022]. Paragraph [0059] indicates that a feed means (Figure 4:42) is provided for supplying cells (Figure 4:59) and that injection channels (Figure 4:44) are provided for supplying

modifiers. The optical trapping aligner device restricts the movement of the cells within a chamber formed by the intersection between the feed means and the injection channels. In Figure 2C, Gruber discloses an embodiment in which a feed means and first and second injection channels intersect to form a reaction chamber. Modified cells are extracted using second feed means (Figure 4:48). Gruber additionally teaches in paragraph [0063] that syringes are used as first and second injection means to deliver modifiers to the first and second injection channels. It is also disclosed in paragraph [0074] that fixing devices (Figure 5:72) are used to stably fix and restrain modified target modification minute objects in the reaction area. Gruber, however, does not clearly state that a carriage is used to align the first and second injection means with the first and second injection channels.

Griner discloses a fluidic device for adding modifiers and other reagents to a biochip. In column 12, lines 15-38, Griner indicates that a plurality of reagent vials (Figure 20:42) are provided with corresponding tubing (Figure 20:154) in communication with various injection ports (Figure 18:158). The injection ports are supported on a carriage (Figure 20:148) that is aligned with each inlet on the biochip.

Gruber and Griner are analogous art because they are from the same field of endeavor regarding microfluidic cell modification apparatuses.

At the time of the invention, it would have been obvious to alter the apparatus and method of Gruber in order to provide each of the injection means on a carriage capable of aligning with each feed means and injection channel. The use of movable injection means provided on a carriage would be beneficial because it would allow one

to add reagents to a plurality of aligner devices using the same injection means. Griner teaches that the attachment of an injection device to a cartridge is desirable because the movement of the cartridge from one aligner device to another can be regulated effectively using an automated control system.

The combination of Gruber and Griner still differs from Applicant's claimed invention because Gruber does not disclose that the aligner device further includes a plurality manipulation electrodes arranged around a recessed hole.

Huang discloses a biochip designed to measure changes in the conductivity of a cell located at a distinct detection site. A recessed hole (Figure 2D:12) is used to trap a cell (Figure 2D:24) at a particular location during testing. This is disclosed in paragraph [0009]. Paragraphs [0031] and [0449] additionally describe the use of a recessed hole surrounded by a plurality of electrodes capable of positioning a target molecule within the hole.

Xu discloses a biochip designed to detect cells on an electrode surface by monitoring impedance. Xu discloses an embodiment in Figure 45 in which a cell moving through an orifice in a thin film is monitored using a plurality of electrodes surrounding the hole.

Gruber, Huang and Xu are analogous art because they are from the same field of endeavor regarding cell evaluation devices capable of trapping a cell at a detection region.

At the time of the invention, it would have been obvious to provide the biochip of Gruber with a recessed hole surrounded by manipulation electrodes capable of trapping a cell within the hole. Huang and Xu each teach that it is known in the art to retain a cell within a recessed orifice, and to subsequently evaluate the cell by measuring changes in impedance while it is located within the orifice. Furthermore, one of ordinary skill in the art would have recognized that cell alignment at a detection region can be aided by applying a suction/negative pressure force to the recessed hole and/or inducing fluid motion through the creation of an electric field using electrodes (see paragraph [0130] of Huang). Accordingly, the use of manipulation electrodes not only would serve to provide information regarding cell conductivity and impedance, but also would provide the operator with another means by which to position a cell at a particular detection site using electro-osmotic forces.

With respect to claim 9, Gruber, Griner and Huang/Xu disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejections above. Gruber additionally indicates in Figure 2 that a plurality of aligner devices are arranged in an array in order to simultaneously modify a plurality of target modification minute objects.

With respect to claim 11, Gruber, Griner and Huang/Xu disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejections above. Gruber further states that the first and second feed means are capillaries with electrodes. Paragraph

[0067] indicates that electrodes are provided within each of the fluid channels in order to create electro-osmotic flow.

2) Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gruber (US 20030119177) in view of Griner (US 5266272) and either Huang (US 20040146849) or Xu (US 7470533) as applied to claim 1, and further in view of Hoffman (US 4989623).

The combination of Gruber, Griner and Huang/Xu discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above, however does not expressly disclose that a recovery mechanism is provided for cleaning and sterilizing the injection means.

Hoffman discloses an apparatus for cleaning the pipette tip of an injection means capable of introducing biological compounds into an analytical system. Hoffman teaches that the pipette tip (Figure 1:4) is automatically moved by a controller to a wash station (Figure 1:10) where the pipette tip is sterilized. This is disclosed in column 2, lines 19-39 and column 3, lines 1-15.

Gruber and Hoffman are analogous art because they are from the same field of endeavor regarding biological analysis systems.

At the time of the invention, it would have been obvious to clean and sterilize the sample injection means disclosed by the combination of Gruber and Griner. Hoffman teaches that disinfecting solutions such as bleach are well known in the art and capable of effectively cleaning an injection device in between uses. Hoffman additionally

teaches that robotic pipette actuation systems are additionally advantageous because they allow one to automatically move an injection means from the analytical apparatus to a wash station.

Response to Arguments

Applicant's arguments filed 14 January 2009 with respect to the 35 U.S.C. 103 rejections of claim 1 under the combination of Gruber and Griner have been fully considered and are persuasive. Therefore, this rejection has been withdrawn. However, upon further consideration, a new ground of rejection is made in view of the combination of Gruber, Griner and either Huang or Xu.

Huang and Xu each address the deficiencies of Gruber by indicating that it is known in the art to position a cell within a recessed hole surrounded by manipulation electrodes. Huang and Xu state that the electrodes can be used to urge a cell toward a recessed hole through the application of an electric field. These references additionally indicate that the manipulating electrodes can also be used to evaluate the cells once positioned within the hole.

Applicant's arguments filed 14 January 2009 with respect to the 35 U.S.C. 103 rejections of claim 13 under the combination of Gruber and Griner have been fully considered but they are not persuasive.

Applicant's principle arguments are

(a) Gruber and Griner do not disclose that first modifiers are injected onto a first surface of the cell, and that second modifiers are injected onto a second surface of the cell.

In response, please consider the following remarks.

It is agreed that Gruber does not disclose the precise placement of a first set of modifiers exclusively at a first cell surface and the precise placement of a second set of modifiers exclusively at a second cell surface. However, this is not required by claim 13. Claim 13 merely states that first modifiers are injected onto a first surface of the cell, and that second modifiers are injected onto a second surface of the cell. This language does not preclude the injection of first modifiers onto the second cell surface as well as the first cell surface. Likewise, this language does not preclude the injection of second modifiers onto the first cell surface as well as the second cell surface. In Gruber, first and second cell modifiers are applied to all surfaces of the captured cell. Therefore, it must be understood that first modifiers are indeed injected onto a first cell surface (as well as other cell surfaces) and that second modifiers are indeed injected onto a second cell surface (as well as other cell surfaces).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/William H. Beisner/
Primary Examiner, Art Unit 1797

/Nathan A Bowers/
Examiner, Art Unit 1797